Acute Coronary Syndrome in 1,366 Patients at Siriraj Hospital: Clinical Characteristics, Management and In-Hospital Outcomes

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Objective: *To characterize the baseline characteristics, management and in-hospital outcomes of all patients admitted with acute coronary syndrome (ACS).*
Material and Method: *The present study is a prospective, observational study of all consecutive patients admitted with ACS. From August 1, 2002 through October 31, 2005, data from 1,366 ACS patients were collected.*
Results: *The patients were classified according to the final discharge diagnosis as ST-segment elevation myocardial infarction (STEMI, 33.5%), non-ST-segment elevation myocardial infarction (NSTEMI, 47%) and unstable angina (UA, 19.5%). Approximately half of the patients were older than 65 years old. The STEMI patients were significantly younger and had a higher percentage of men than the NSTE-ACS patients. There was a very high prevalence of diabetes, hypertension and dyslipidemia in the patients. Only 60% of the STEMI patients received reperfusion therapy. Of these, primary percutaneous coronary intervention (PCI) was performed more frequently (35%) than thrombolytic therapy (24%). There were substantial delays in time to treatment. Median door to needle and door to balloon time were 135 and 130 minutes respectively. Half of the NSTEMI and UA patients underwent coronary angiography and about one-third had PCI or coronary artery bypass grafting in the same hospital admission. In-hospital mortality rate was high: STEMI 19%, NSTEMI 16% and UA 4%.*
Conclusion: *The present study provides invaluable information regarding the spectrum of ACS in our country. Overall in-hospital mortality was higher than that reported from international registries. The present findings represent a significant opportunity for quality improvement in the care of patients with ACS and the implementation of preventive strategies for patients with and at risk for coronary artery disease.*

Keywords: *Acute coronary syndrome, ST-segment elevation myocardial infarction, Non-ST-segment elevation myocardial infarction, Unstable angina*

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Acute coronary syndrome (ACS) represents a continuum of acute myocardial ischemia and includes ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina. Thus, ACS includes a heterogeneous spectrum of conditions that result in a major cause of morbidity and mortality worldwide. In Thailand, there are limited data on patients with ACS. The present study is a prospective, observational study to characterize the baseline characteristics, management and in-hospital outcomes of all patients within

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the entire spectrum of ACS who were admitted to Siriraj Hospital over a three-year period. These results may provide important data for future improvement in the management and outcomes of ACS in Thailand.

Material and Method

From August 1, 2002 through October 31, 2005, data from all patients who were admitted to Siriraj Hospital with a final diagnosis of ACS were collected prospectively and consecutively. Patients who presented within 14 days of chest pain or other symptoms suggestive of ACS were enrolled. Data from 1,366 patients with ACS were collected.

Patients were categorized into three groups according to their final diagnosis as follows 1) ST-segment elevation MI (STEMI) 2) Non-ST-segment elevation MI (NSTEMI) 3) Unstable angina (UA) with ST-T wave changes.

STEMI was diagnosed by having elevated biochemical markers of myocardial necrosis and ECG changes demonstrating either 1) ST-segment elevation $\geq$ 1 mm in two consecutive leads or 2) new or presumed new left bundle branch block. NSTEMI was determined by evidence of elevated biochemical markers of myocardial necrosis and either 1) ischemic symptoms compatible with ACS or 2) ST-segment depression or T wave abnormalities. Unstable angina was defined as having ischemic symptoms compatible with ACS and ST-segment depression or T wave abnormalities.

Data collection

Patient clinical, demographic, treatment and outcome data were collected by cardiac nurses and transcribed onto standard data forms.

Demographic variables included gender and age. Dyslipidemia, diabetes, hypertension, history of tobacco use and family history were used to characterize risk factors. Diabetes was diagnosed when the patient's fasting plasma glucose was 126 mg/dl or higher on at least two occasions or there was the presence of a history of diabetes treated with either dietary control or antidiabetic medication. Hypertension was defined as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg or a previous diagnosis of hypertension. Dyslipidemia was diagnosed when total cholesterol was > 200 mg/dl, LDL cholesterol > 130 mg/dl, HDL cholesterol < 40 mg/dl or there was a previous diagnosis of dyslipidemia and/or currently being treated with a lipid-lowering agent. Tobacco use was defined by the habitual use of tobacco within two years of index hospital admission.

Presenting symptoms were recorded as typical angina, atypical angina, dyspnea, cardiogenic shock, congestive heart failure and cardiac arrest. Typical angina was defined as chest pain typical of myocardial ischemia (chest, arm or jaw pain/pressure aggravated by exertion or stress, and relieved by rest or nitroglycerine). Atypical angina was chest pain that could not be characterized as typical angina. Cardiogenic dyspnea was noted if the patient had shortness of breath on exertion, and/or orthopnea, and/or paroxysmal nocturnal dyspnea. Palpitation was defined as the patient's sense of abnormal heart rhythm. Syncope was defined as transient loss of consciousness with spontaneous recovery without neurological deficit. Congestive heart failure was defined as bibasilar rales in $\leq$ 50% of lung fields or the presence of an S3 gallop (Killip II), or bibasilar rales in > 50% of lung fields (Killip III). Cardiogenic shock (Killip class IV) was defined as symptomatic hypoperfusion with systolic blood pressure < 90 mm Hg. Payer status of the patient was collected as follows: civil servant reimbursement, 30 Baht Universal Health Care, social service insurance, self paid or others.

Reperfusion strategy in STEMI included use of thrombolytic therapy, primary percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG). Procedural data included coronary angiography, CABG and PCI. Medical management included the use of aspirin, thienopyridine, heparin, low-molecular weight heparin, GP IIb/IIIa antagonist, angiotensin-converting inhibitor, beta-blockers, calcium channel blocker, angiotensin receptor blocker, nitrates and statins.

In-hospital complications included major bleeding, congestive heart failure, cardiogenic shock, arrhythmia, stroke, and death. Cardiac arrhythmia was classified as heart block (at least 2nd degree AV block) or ventricular arrhythmia (sustained ventricular tachy-

Table 1. Relation between initial diagnosis on admission and final diagnosis

Initial Diagnosis	Final diagnosis, Number (%)			Total
	STEMI	NSTEMI	UA	
STEMI	439 (95.9)	7 (1.1)	4 (1.5)	450
NSTEMI	17 (3.7)	614 (95.6)	1 (0.4)	632
UA	2 (0.4)	21 (3.3)	261 (981)	284
Total	458	642	266	1,366

cardia or ventricular fibrillation). In-hospital death was categorized as cardiac or non-cardiac death.

This protocol was approved by the hospital ethics committee and is in accordance with the Declaration of Helsinki. Verbal consent was obtained from every patient.

Statistical analysis

Categorical data were summarized as frequencies and percentages. Continuous variables were reported as mean ± SD or median and 25th and 75th percentiles. Differences between patient groups were examined using Chi-square tests for categorical variables. Differences in continuous variables between groups were analyzed using either analysis of variance or t tests. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) Windows version 11.5. All tests were double-sided and considered statistically significant at $p < 0.05$.

Results

During the 3-year period, 1,366 patients with ACS were enrolled. The patients were characterized into three groups according to the final diagnosis: STEMI 458 (33.5%) patients, NSTEMI 642 (47%) patients and UA 266 (19.5%) patients.

Table 1 demonstrates that the majority of patients had an initial diagnosis that was concordant with

Table 2. Payer status of all acute coronary syndrome patients

	Total ACS patients n (%)	UA n (%)	NSTEMI n (%)	STEMI n (%)	p-value
30 Baht universal health care	292 (39.8)	51 (36.2)	155 (40.9)	86 (40.4)	0.519
Civil servant reimbursement	339 (46.2)	73 (51.8)	169 (44.6)	97 (45.5)	
Social service insurance	22 (3)	4 (2.8)	8 (2.1)	10 (4.7)	
Self paid	60 (8.2)	11 (7.8)	34 (9)	15 (7)	
Others	20 (2.7)	2 (1.4)	13 (3.4)	5 (2.3)	

Table 3 Baseline characteristics of the patients stratified by discharge diagnosis

	UA n (%) n =266	NSTEMI n (%) n = 642	STEMI n (%) n = 458	p-value
Age, mean SD (yrs)	67.9 ± 10.7	69 ± 10.7	63.2 ± 12.8	<0.001
Male gender	121 (45.5)	338 (52.6)	302 (65.9)	<0.001
Medical history				
Diabetes	131 (50)	336 (53)	173 (39.2)	<0.001
Hypertension	208 (78.2)	495 (77.5)	253 (56.6)	<0.001
Dyslipidemia	218 (85.8)	493 (81.2)	331 (77.2)	0.02
Tobacco use	54 (20.4)	130 (20.5)	175 (38.8)	<0.001
Family history of coronary artery disease	31 (11.7)	50 (7.8)	70 (15.3)	0.001
Previous myocardial infarction	20 (28.6)	56 (27.7)	19 (14.3)	0.007
Referred	42 (16)	113 (17.6)	187 (40.9)	<0.001
Ejection fraction (mean, %)	60.6 ± 12.9	52.3 ± 15.9	51.9 ± 16.2	0.01
Body mass index (mean, kg/m^2)	24.8 ± 3.4	23.5 ± 3.7	24.1 ± 3.8	0.066
Presenting symptom				
Chest pain	248 (93.2)	483 (75.2)	398 (86.9)	<0.001
Typical angina	165 (84.6)	316 (68)	320 (84.7)	<0.001
Atypical angina	19 (9.7)	44 (9.5)	16 (4.2)	0.008
Dyspnea	77 (39.3)	225 (51.1)	89 (27.4)	<0.001
Shock	6 (2.3)	31 (4.8)	58 (12.7)	<0.001
Cardiac arrest	4 (1.5)	18 (2.8)	27 (5.9)	0.003
Congestive heart failure	104/266 (39.1)	393/642 (61.2)	183/458 (40)	<0.001

their final diagnosis. One-quarter (342) of the patients were referred to Siriraj Hospital. STEMI patients were more frequently referred (40.9%) than the NSTEMI-UA group. The majority of ACS patients admitted to the hospital (table 2) received civil servant reimbursement (46%) or were under the 30 Baht Universal Health Care reimbursement program (40%).

The baseline characteristics and risk factors of the patients are shown in Table 3. Approximately half of the patients were older than 65 years old. Patients who presented with STEMI were significantly younger than those who presented with NSTEMI or UA. Men were predominant in STEMI, whereas a greater proportion of UA patients were women.

There was an alarmingly high prevalence of diabetes, hypertension and dyslipidemia. In the STEMI patients, a history of tobacco use was significantly more frequent, whereas diabetes, hypertension and dyslipidemia were less frequent. The mean left-ventricular ejection fraction was preserved overall but lowest in the STEMI group.

Presenting symptoms varied significantly among the three diagnoses. Up to 25% of NSTEMI patients did not have chest pain. Dyspnea and congestive heart failure were frequently present on admission. In the STEMI group, cardiogenic shock and cardiac arrest were significantly more common than the NSTEMI-UA group.

Pharmacological treatments during the hospitalization are listed in Table 4. Aspirin was almost uniformly prescribed. The STEMI patients received thienopyridines (clopidogrel or ticlopidine) more frequently. For antithrombin therapy, low molecular weight heparin (LMWH) was utilized more frequently than unfractionated heparin particularly in the NSTEMI-UA patients. Platelet glycoprotein IIb/IIIa antagonists were infrequently used. Approximately 60-70% of patients received beta-blockers and angiotensin converting enzyme inhibitors. Statins were given to nearly 90% of the patients.

Table 5 characterizes the invasive management of ACS during the hospitalization. Coronary an-

Table 4. Pharmacologic therapy during the hospitalization

Medication	UA n (%) n = 266	NSTEMI n (%) n = 642	STEMI n (%) n = 458	p-value
Aspirin	249 (93.6)	604 (94.1)	444 (96.9)	0.246
Thienopyridine	38 (54.3)	106 (52.5)	102 (76.7)	<0.001
Low molecular weight heparin	211 (79.3)	517 (80.5)	181 (39.5)	<0.001
Unfractionated heparin	13 (4.9)	74 (11.5)	133 (29)	<0.001
GP IIb/IIIa antagonist	1 (0.4)	12 (1.9)	44 (9.6)	<0.001
Beta-blocker	51 (72.9)	139 (68.8)	82 (61.7)	0.211
Angiotensin converting enzyme inhibitor	179 (67.3)	381 (59.3)	301 (65.7)	0.027
Angiotensin receptor blocker	36 (13.5)	54 (8.4)	24 (5.2)	0.001
Statin	238 (89.5)	555 (86.4)	383 (83.6)	0.085
Calcium channel blocker	66 (24.8)	173 (26.4)	32 (7)	<0.001
Nitrate	245 (92.1)	560 (87.2)	313 (68.3)	<0.001

Table 5. Invasive management during the hospitalization

Treatment	UA n (%) n = 266	NSTEMI n (%) n = 642	STEMI n (%) n = 458	p-value
Coronary angiography performed	122 (45.9)	278 (43.3)	336 (73.4)	< 0.001
Abnormal findings	103 (84.4)	267 (96)	326 (97)	< 0.001
Revascularization				
Percutaneous coronary intervention	63 (23.7)	142 (22.1)	274 (59.8)	< 0.001
CABG	22 (8.3)	86 (13.4)	39 (8.5)	< 0.001
: Emergency CABG	5 (1.9)	24 (3.7)	15 (5.2)	
: Elective CABG	17 (6.4)	62 (9.7)	15 (3.3)	

giography was performed more frequently (73%) in the STEMI patients than the NSTE-ACS patients (45%). Accordingly, a higher proportion of the STEMI patients underwent percutaneous coronary intervention (PCI). A small percentage of patients from all groups underwent coronary artery bypass graft (CABG) surgery.

Specific treatment data in the STEMI patients are shown in Table 6. Approximately 75% of the patients had an indication for thrombolytic therapy, nevertheless, less than 60% of the patients received reperfusion therapy. Among these patients, 24% received thrombolysis and 35% underwent primary PCI. Streptokinase was the lytic agent used in 90% of all cases. When the referred patients were excluded, thrombolytic therapy was initiated at a median delay (door-to-needle time) of 135 minutes. Likewise, in the primary PCI treated patients, the median door to balloon delay time was 130 minutes.

In-hospital mortality (Table 7) was 14.6% in the entire ACS cohort. Mortality rate was significantly much higher in patients with STEMI than NSTEMI and UA (19%, 16% and 4%, respectively). The majority of deaths were categorized as cardiac deaths.

The mean length of stay was significantly longer in the NSTEMI patients than STEMI and UA patients (15.6, 11.2, 11.4 days, respectively).

Discussion

In the present study, the authors used observational data on patients admitted with ACS to report the baseline characteristics, management and in-hospital outcomes according to the specific type of ACS in real-world clinical practice at our institute. NSTEMI was the most frequent diagnosis (up to 47%) followed by STEMI, 33.5%, and UA, 19.5%. The majority of patients had an initial diagnosis that was concordant with their final diagnosis.

Table 6. Treatment in ST-Segment elevation myocardial infarction patients

Treatment	Number (%)	Medium	Min, Max	Mean ± SD
Reperfusion therapy	269 / 458 (58.7)			
Thrombolysis	111 / 458 (24.2)			
Tissue plasminogen activator	6 / 51 (11.8)			
Streptokinase	45 / 51 (88.2)			
Door to needle time, min		135	10, 230	136.3 ± 10
Onset to treatment time, min		280	90, 720	284.8 ± 20.4
Primary PCI	158 / 458 (34.5)			
Door to balloon time, min		130	13, 1328	195.5 ± 21.4
Onset to treatment time, min		326	73, 1405	416.4 ± 29.4
Rescue PCI	25 / 458 (5.5)			
Emergency CABG	24 / 458 (5.2)			
Elective PCI	91 / 458 (19.9)			
Elective CABG	15 / 458 (3.3)			

Table 7. In-hospital outcomes

Outcome	UA n (%)	NSTEMI n (%)	STEMI n (%)	Total ACS n (%)	p-value
Congestive heart failure	3/107 (2.8)	18/409 (4.4)	11/193 (5.7)	32/711 (4.5)	0.509
Serious cardiac arrhythmia	14/264 (5.3)	71/640 (11.1)	131/458 (28.6)	216/1366 (15.8)	<0.001
Stroke	6/261 (2.3)	11/642 (1.7)	15/455 (3.3)	32/1358 (2.3)	0.239
Major bleeding	8/266 (3)	35/636 (5.5)	33/458 (7.2)	76/1360 (5.6)	0.059
Death	10/266 (3.8)	101/642 (15.7)	89/458 (19.4)	200/1366 (14.6)	<0.001
Cardiac death	9/266 (3.4)	48/642 (7.5)	66/458 (14.4)	123/1366 (9)	<0.001
Non cardiac death	1/266 (0.4)	53/642 (8.3)	23/458 (5)	77/1366 (5.6)	<0.001
Length of stay (days),mean ± SD	11.4 ± 10.6	15.6 ± 14.7	11.2 ± 15.7		<0.001

Patients under civil servant reimbursement represented half of the presented ACS population and 40% of the patients were under the 30 Baht Universal Health Care scheme. Payer status is an important patient factor. Studies from the US[1] have reported that NSTEMI patients with different types of insurance coverage particularly in people with low income were less likely to receive evidence-based therapies and had worse outcomes than patients with other types of insurance. The causes of these treatment differences are unclear and require further investigation particularly in our patient population.

Surprisingly, there were a high percentage of women in the UA patients (55%) and in the NSTEMI patients (47%). This percentage is higher than that reported from international[2] and US ACS registries[3] of which women represented only 30-40%. Gender related differences in the diagnosis, treatment and outcome of ACS have been well-described[3]. The authors were unable to discern whether our ACS patients truly comprised of more women or if this was a selection bias of admitting more women due to their higher risk profile. This is a limitation of the present analysis.

The presence of diabetes was remarkably high up to 50% in the NSTE-ACS patients. Reported percentage of diabetics from international registries of ACS range from 19-32%[2-4]. These findings have substantial national health implications as diabetes has been consistently shown to have an adverse effect on survival in acute myocardial infarction patients[5-6].

Pharmacologic therapies that improve outcome such as aspirin, beta-blockers, statins, angiotensin-converting enzyme inhibitor were frequently used. Conversely, despite the evidence of benefit of GP IIb/IIIa antagonists in ACS[7,8], these drugs were used in less than 10% of the patients. The reason for this in unclear and could be, in part, due to their high cost.

Utilization of invasive procedures such as coronary angiography and percutaneous coronary intervention were high and comparable to those reported from GRACE[2]. In the STEMI patients, only 60% of the patients received reperfusion therapy. Primary PCI was performed more frequently than thrombolysis. This may seem reassuring, given that randomized trials have documented the superiority of primary PCI over thrombolysis regarding hospital mortality[9]. However, in the primary PCI treated patients the delay from admission to PCI was substantial, 130 minutes. Likewise, the median delay time to initiation of lytics (door to needle time) was 135 minutes. The current published guidelines recommends a door-to-needle time $\leq$ 30 minutes for thrombolytic therapy and door-to-balloon time $\leq$ 90 minutes for primary angioplasty[7,10]. Thus, the presented time to treatment is far exceeding the length of time recommended.

The overall in-hospital mortality rate for the presented patients was considerably high (STEMI 19.4%, NSTEMI 15.7%) compared to GRACE[2] (STEMI 7%, NSTEMI 5%). Compared with the patients in GRACE, the presented patient population had a higher percentage of diabetics, women and had substantially longer time from presentation to treatment. All of these have been consistently associated with poorer clinical outcome[3,5,6,11-13]. It is noteworthy, that as Siriraj Hospital is a tertiary care center and a quarter of the patients were referrals it is plausible, there may have been a selection bias which resulted in transferring sicker patients to the hospital.

Limitations

This is an analysis of an observational database from a single tertiary care institute, not a population-based epidemiological study. Thus, the present findings may not be representative of the universe of ACS patients in Thailand. All ACS patients that required hospitalization may not have been captured. Very ill patients who died during the first 24 hours after admission may have been excluded. At the other end of the spectrum, the lower risk patients with NSTE-ACS that were managed in the observation unit of the emergency department would not have been captured.

The present study provides invaluable information to enable physicians, patients, hospitals and health-care policy makers to become aware of the true burden of ACS in Thailand. In addition, the present findings represent a significant opportunity to make changes directed towards quality improvement in the care of patients with ACS, as well as the implementation of preventive strategies for patients with, and at risk for, coronary artery disease.

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ภาวะกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันในผู้ป่วย 1,366 รายที่โรงพยาบาลศิริราช : ลักษณะทางคลินิก การรักษา และผลลัพธ์ที่เกิดขึ้นในโรงพยาบาล

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วัตถุประสงค์: *เพื่อรายงานลักษณะทางคลินิกของผู้ป่วย การรักษาและผลลัพธ์ที่เกิดขึ้นในโรงพยาบาล ในผู้ป่วยทุกรายที่รับไว้ในโรงพยาบาลด้วยภาวะกล้ามเนื้อหัวใจขาดเลือดเฉียบพลัน (ACS)*

วัสดุและวิธีการ: *การศึกษานี้เป็นการเก็บรวบรวมทะเบียนผู้ป่วยแบบไปข้างหน้าของผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันทุกราย ตั้งแต่เดือนสิงหาคม พ.ศ.2545 ถึง ตุลาคม พ.ศ.2548*

ผลการศึกษา: *มีจำนวนผู้ป่วยทั้งหมด 1,366 ราย ผู้ป่วยได้รับการแยกแยะเป็น 3 กลุ่มโรค ตามการวินิจฉัยขั้นสุดท้าย ได้แก่ ST-segment elevation myocardial infarction (STEMI) 33.5%, non-ST-segment elevation myocardial infarction (NSTEMI) 47% และ unstable angina (UA) 19.5% ประมาณครึ่งหนึ่งของผู้ป่วยอายุมากกว่า 65 ปี ผู้ป่วย STEMI อายุน้อยกว่า และเป็นผู้ชายมากกว่า ในผู้ป่วยกลุ่ม NSTE-ACS มีผู้ป่วยที่มีโรคเบาหวาน ความดันโลหิตสูง และไขมันในเลือดสูง เป็นโรคร่วมเป็นจำนวนมาก ในผู้ป่วยกลุ่ม STEMI 60% ได้รับการรักษาเพื่อเปิดหลอดเลือด ในจำนวนนี้ 35% ได้รับการทำ primary percutaneous coronary intervention (PCI) และ 24% ได้รับ thrombolytic therapy ค่ามัธยฐานเวลา door to needle time 135 นาที และ door to balloon time 130 นาที ในผู้ป่วยกลุ่ม NSTEMI และ UA ประมาณครึ่งหนึ่ง ได้รับการฉีดสีดูหลอดเลือดหัวใจและหนึ่งในสามได้รับการทำ PCI หรือการผ่าตัดบ่ายเบนหลอดเลือดหัวใจ ขณะอยู่ใน โรงพยาบาล อัตราการเสียชีวิตในโรงพยาบาลค่อนข้างสูง ดังนี้ 19% ในผู้ป่วย STEMI 16% ในผู้ป่วย NSTEMI และ 4% ในผู้ป่วย UA*

สรุป: *การศึกษานี้ ให้รายละเอียดข้อมูลที่สำคัญเกี่ยวกับผู้ป่วยคนไทยที่เป็น ACS ทุกชนิด พบว่าอัตราการเสียชีวิตของผู้ป่วยในโรงพยาบาลสูงกว่าข้อมูลของต่างประเทศ ข้อมูลเหล่านี้สามารถใช้เป็นแนวทางในการพัฒนาการดูแลผู้ป่วยกลุ่มนี้ เพื่อปรับปรุงผลลัพธ์ในการรักษา และเพื่อพิจารณาป้องกันโรคหลอดเลือดหัวใจ*